

PATENT COOPERATION TREATY


CONFIRMATION

From the:
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

| |
|--|
| To:  James & Wells PO Box 2201 Christchurch NEW ZEALAND |
|--|

| | |
|-------------------------------------|-------------|
| Date of mailing (day/month/year) | 18 NOV 2004 |
|-------------------------------------|-------------|

| |
|--|
| Applicant's or agent's file reference 42968PCX329 |
|--|

| |
|--|
| FOR FURTHER ACTION See paragraph 2 below |
|--|

| | | |
|---|--|--|
| International application No. PCT/NZ2004/000184 | International filing date (day/month/year) 13 August 2004 | Priority date (day/month/year) 15 August 2003 |
|---|--|--|

| |
|--|
| International Patent Classification (IPC) or both national classification and IPC Int. Cl. ⁷ A61K 31/407; A61P 9/10, 9/12 |
|--|

| |
|--|
| Applicant AGRESEARCH LIMITED et al |
|--|

1. This opinion contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion |
| <input type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input checked="" type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

| | |
|---|--|
| Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustrialia.gov.au Facsimile No. (02) 6285 3929 | Authorized Officer S. CHEW Telephone No. (02) 6283 2248 |
|---|--|

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/NZ2004/000184

Box No. I Basis of the opinion

1. ☒ With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
- a. type of material
- ☐ a sequence listing
- ☐ table(s) related to the sequence listing
- b. format of material
- ☐ in written format
- ☐ in computer readable form
- c. time of filing/furnishing
- ☐ contained in the international application as filed.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/NZ2004/000184

Box No. V

Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|------------------------------|-----|
| Novelty (N) | Claims 9, 11, 14-15, 35-36 | YES |
| | Claims 1-8, 10, 12-13, 16-34 | NO |
| Inventive step (IS) | Claims 9, 11, 14-15, 35-36 | YES |
| | Claims 1-8, 10, 12-13, 16-34 | NO |
| Industrial applicability (IA) | Claims 1-36 | YES |
| | Claims | NO |

2. Citations and explanations:

This report has considered the following documents cited in the International Search Report:

- D1 WO 2003/105868
- D2 Miles C. et al.
- D3 Munday-Finch S. et al. J. Agric. Food Chem. 1995
- D4 Munday-Finch S. et al. J. Agric. Food Chem. 1998
- D5 Munday-Finch S. et al. J. Agric. Food Chem. 1997
- D6 Derwent Abstract Accession No. 92-308267/38
- D7 Munday-Finch S. et al. J. Agric. Food Chem. 1996

NOVELTY (N) : Claims 1-8, 10, 12-13, 16-34

The composition claims are considered to be directed to compositions which are characterised by their components only, that is compounds having the structure as defined. The term "BK channel antagonist" does not limit the scope of the claims. Thus any document which discloses compounds having the defined structure would anticipate the composition claims.

D1 was published after the priority date and will not be considered further. See however the indications in Box VI.

D2 has disclosed the isolation and structures of lolitrems B and E including their biosynthetic route from lolitriol (see abstract and figure 1). Therefore claims 1-5, 7, 16-29 and 33-34 are not novel.

D3 has disclosed the isolation of lolitrem A, its structure and structures of lolitrems B, C and E (see abstract and figure 1). Therefore claims 1-6, 16-26 and 33-34 are not novel.

D4 has disclosed the isolation of lolicines A and B, lolitriol and lolitrem N and has provided evidence for 31-epilolitrem N and 31-epilolitrem F (see abstract and figure 1). Therefore claims 1-7, 12-13 and 16-34 are not novel.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/NZ2004/000184

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

| <u>Application No. Patent No.</u> | <u>Publication date (day/month/year)</u> | <u>Filing date (day/month/year)</u> | <u>Priority date (valid claim) (day/month/year)</u> |
|---------------------------------------|--|---|---|
| P,X WO 2003/105868 | 24 December 2003 | 13 June 2003 | 17 June 2002 |

This document has disclosed lolitrems A, B, C, E, F, H, N, lolitrem N-31-epimer, lolitriol, lolilline, lolitriol, lolicines A and B and their use as potassium channel blockers for the treatment of ocular hypertension or glaucoma (see pages 5, 7, 13 and claim 1). Therefore claims 1-8, 10, 12-13, 16-34 are not novel.

With regard to the document(s) listed in Box VI under "certain documents cited", these are documents published prior to the international filing date but later than the priority date claimed but which would otherwise be considered to be of particular relevance.

Under the PCT, novelty is considered only in respect of documents published before the priority date. The relevance of a document published after the priority date is dependent upon national law. Such documents are excluded from consideration in preliminary examination, under the PCT Guidelines but have been included here for information.

2. Non-written disclosures (Rules 43bis.1 and 70.9)

| <u>Kind of non-written disclosure</u> | <u>Date of non-written disclosure (day/month/year)</u> | <u>Date of written disclosure referring to non-written disclosure (day/month/year)</u> |
|---------------------------------------|--|--|
|---------------------------------------|--|--|

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International Application No.

PCT/NZ2004/000184

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V

D5 has disclosed lolilline, lolitrems A, B, E and lolitriol (see figures 1 and 3). Therefore claims 1-7, 10, 16-29 and 33-34 are not novel.

D6 has disclosed lolitrem derivatives which fall within the scope of the compounds of claims 1-3, 7 and 16-24.

D7 has disclosed lolitrem F, lolitrem B, 31-epilolitrem B, 31-epilolitrem F and lolitriol (see abstract, figures 1 and 4). Therefore claims 1-4, 16-32 and 34 are not novel.

INVENTIVE STEP (IS): Claims 1-8, 10, 12-13, 16-34

AS above.

INDUSTRIAL APPLICABILITY (IA): Claims 1-36

Claims 1-36 have industrial applicability.